



**A.G.E.O.**

ASSOCIAZIONE GINECOLOGI EXTRA OSPEDALIERI

3° CORSO DI AGGIORNAMENTO IN  
**GINECOLOGIA E OSTETRICIA**

BOLOGNA 22-23 NOVEMBRE 2019

Presidente del Corso: *Claudio Zanardi*



ALMA MATER STUDIORUM  
UNIVERSITÀ DI BOLOGNA

# Miomectomy isteroscopica e laparoscopica: outcome riproduttivo

Renato Seracchioli



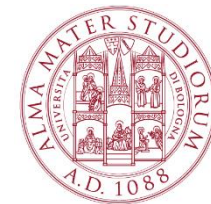
**ALMA MATER STUDIORUM – UNIVERSITÀ DI BOLOGNA - ITALY**

# Surgical approach to Uterine Myomas in women with reproductive expectancies

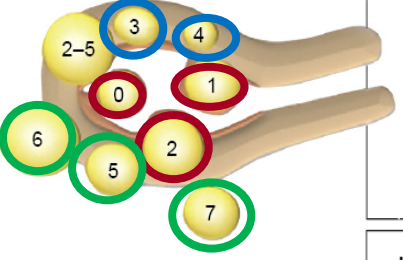
- Myomas and fertility.
- Does myomectomy improve fertility outcomes
- Does myomectomy improve IVF outcomes
- Surgical technique?
- Strategies to improve our surgery
- And after surgery? Pregnancy after myomectomy



# Impact on fertility



**Leiomyoma subclassification system**



<b>SM – Submucosal</b>	0	Pedunculated intracavitary
	1	<50% intramural
	2	≥50% intramural
<b>O – Other</b>	3	Contacts endometrium; 100% intramural
	4	Intramural
	5	Subserosal ≥50% intramural
	6	Subserosal <50% intramural
	7	Subserosal pedunculated
	8	Other (specify eg, cervical, parasitic)
<b>Hybrid leiomyomas (impact both endometrium and serosa)</b>		Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium, while the second refers to the relationship to the serosa. One example is given below
	2–5	Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively

**Figure 1** FIGO leiomyoma subclassification system.  
**Note:** Reprinted from *Int J Gynaecol Obstet*. Vol 113(1). Munro MG, Critchley HO, Broder MS, Fraser IS, FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nonpregnant women of reproductive age. Pages 3–13. Copyright 2011, with permission from Elsevier.  
**Abbreviation:** FIGO, International Federation of Gynecology and Obstetrics.

**SUBMUCOSAL**

**INTRAMURAL**



**SUBSEROSAL**

SOGC CLINICAL PRACTICE GUIDELINE

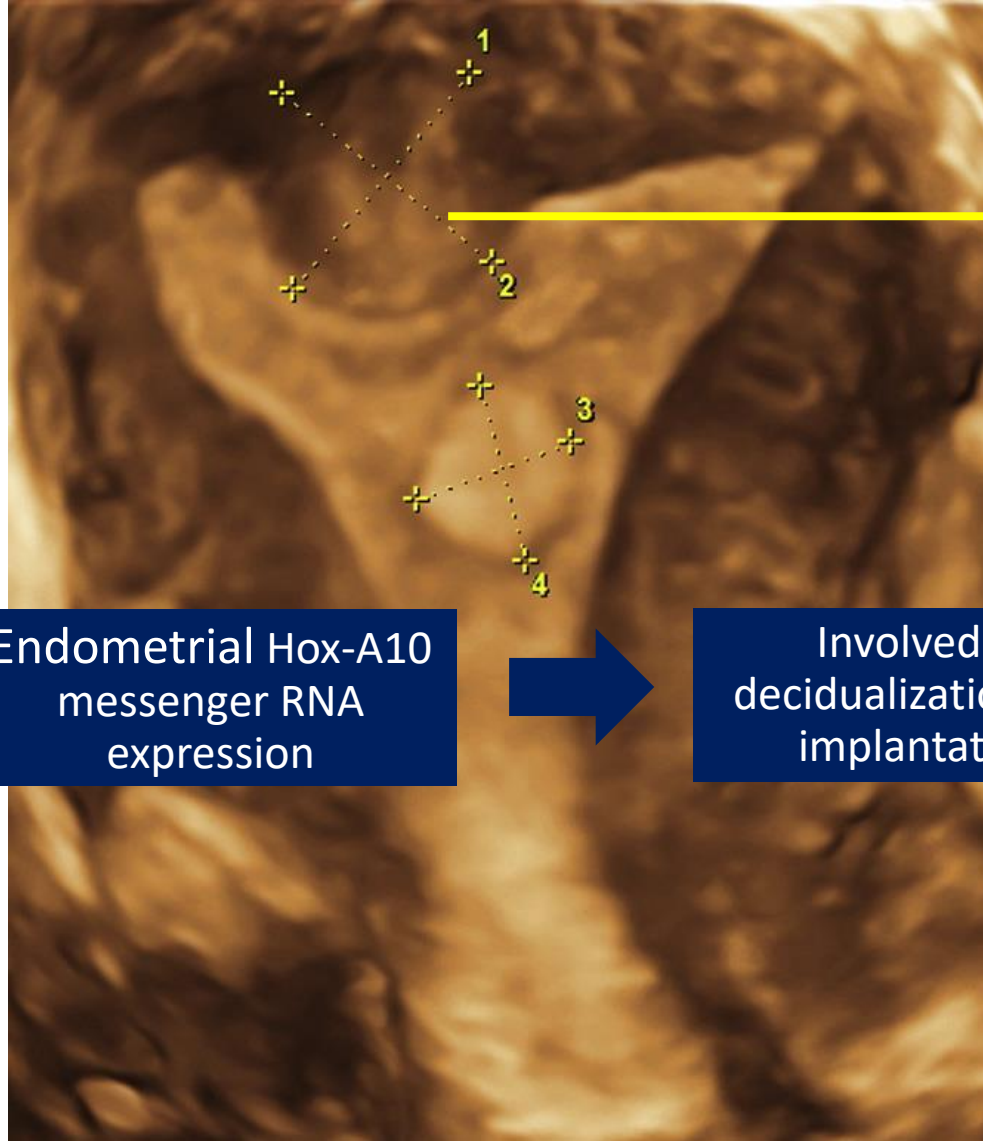
No. 321, March 2015

**The Management of Uterine Fibroids in Women With Otherwise Unexplained Infertility**

- Subserosal fibroids do not appear to have an impact on fertility
- All systematic reviews and meta-analyses agreed on this point.
- Removal of subserosal fibroids is not recommended. (III-D)



# Impact on fertility

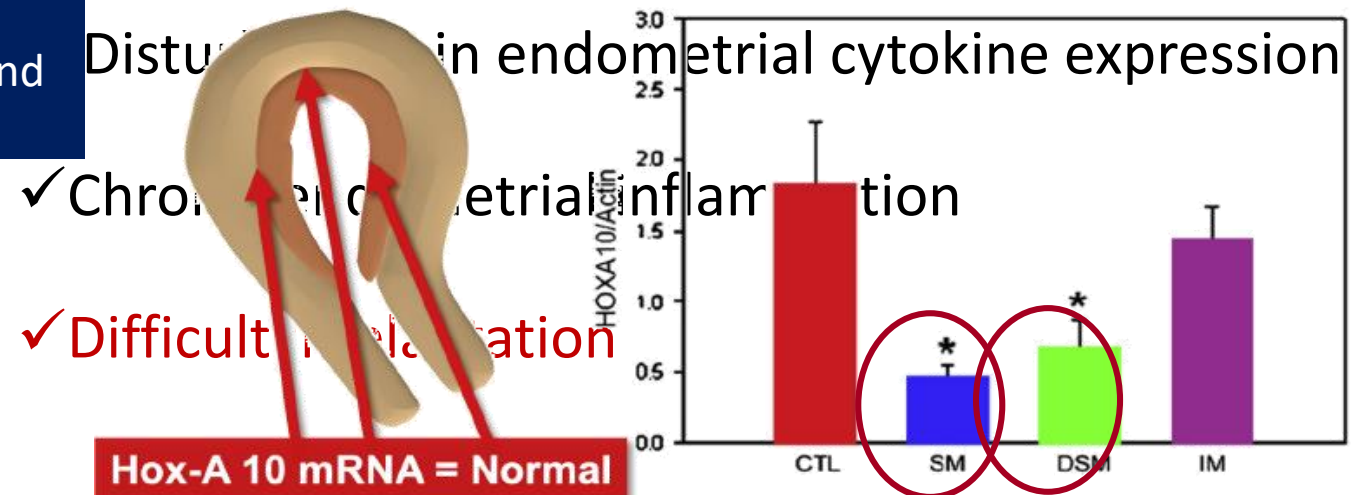
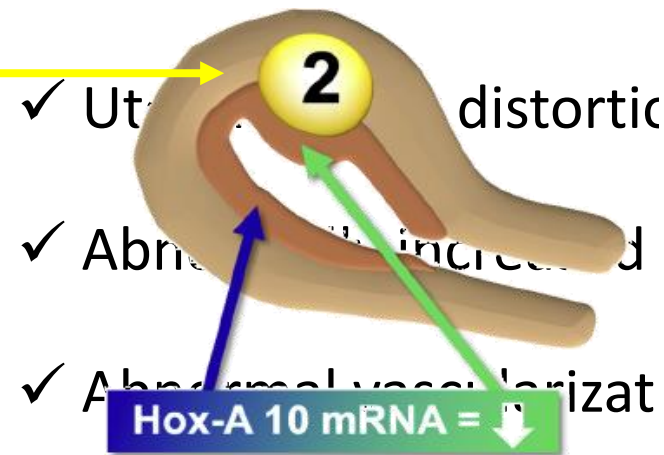


Endometrial Hox-A10 messenger RNA expression



Involved in decidualization and implantation

SUBMUCOSAL



# Impact on fertility

## Fibroids and infertility: an updated systematic review of the evidence

Elizabeth A. Pritts, M.D.,<sup>a</sup> William H. Parker, M.D.,<sup>b</sup> and David L. Olive, M.D.<sup>a</sup>

2009

**TABLE 2**

Effect of fibroids on fertility: all locations.

Outcome	Number of studies/substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	18	0.849	0.734–0.983	$P = .029$
Implantation rate	14	0.821	0.722–0.932	$P = .002$
Ongoing pregnancy/live birth rate	17	0.697	0.589–0.826	$P < .001$
Spontaneous abortion rate	18	1.678	1.373–2.051	$P < .001$
Preterm delivery rate	3	1.357	0.607–3.036	Not significant

*Pritts. Fibroids and infertility. Fertil Steril 2009.*

**TABLE 3**

Effect of fibroids on fertility: submucous fibroids.

Outcome	Number of studies/substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	4	0.363	0.179–0.737	$P = .005$
Implantation rate	2	0.283	0.123–0.649	$P = .003$
Ongoing pregnancy/live birth rate	2	0.318	0.119–0.850	$P < .001$
Spontaneous abortion rate	2	1.678	1.373–2.051	$P = .022$
Preterm delivery rate	0	—	—	—

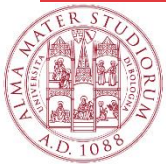
*Pritts. Fibroids and infertility. Fertil Steril 2009.*

**TABLE 4**

Effect of fibroids on fertility: no intracavitary involvement.

Outcome	Number of studies/substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	24	0.897	0.800–1.004	Not significant
Implantation rate	14	0.792	0.696–0.901	$P < .001$
Ongoing pregnancy/live birth rate	16	0.780	0.690–0.883	$P < .001$
Spontaneous abortion rate	16	1.891	1.473–2.428	$P < .001$
Preterm delivery rate	2	2.767	0.797–9.608	Not significant

*Pritts. Fibroids and infertility. Fertil Steril 2009.*



# Impact on fertility

## Fibroids and female reproduction: a critical analysis of the evidence

Human Reproduction Update, Vol.13, No.5 pp. 465–476, 2007  
Advance Access publication June 21, 2007

E. Somigliana<sup>1,2</sup>, P. Vercellini<sup>1,2,3,4</sup>, R. Daguati<sup>1,2,3</sup>, R. Pasin<sup>1,3</sup>, O. De Giorgi<sup>1,2</sup> and P.G. Crosignani<sup>1,3</sup>

**Table 3:** Meta-analyses on the influence of fibroids on IVF outcome according to the localization of the lesions

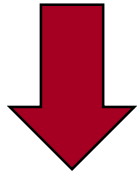
Localization	Number of studies included <sup>a</sup>	Breslow–Day test ( <i>P</i> -value)	Common OR (95% CI)
<b>Clinical pregnancy rate</b>			
Submucosal	2	0.92	0.3 (0.1–0.7)
Intramural	7	0.38	0.8 (0.6–0.9)
Subserosal	3	0.92	1.2 (0.8–1.7)
Intramural and/or subserosal	11	0.30	1.0 (0.8–1.2)
All types	16	0.24	0.8 (0.7–1.0)
<b>Delivery rate</b>			
Submucosal	2	0.79	0.3 (0.1–0.8)
Intramural	7	0.09	0.7 (0.5–0.8)
Subserosal	3	0.94	1.0 (0.7–1.5)
Intramural and/or subserosal	11	0.68	0.9 (0.7–1.1)
All types	16	0.43	0.8 (0.6–0.9)

### PREGNANCY RATE

- Submucosal → big impact
- Intramural → low impact
- Subserosal → no impact

# Impact on fertility

SUBMUCOSAL

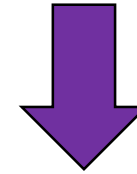


Definite impact on fertility

INTRAMURAL



SUBSEROUSAL



No impact on fertility



# Fibroids and infertility: an updated systematic review of the evidence 2009

First meta-analysis

TABLE 5

Effect of fibroids on fertility: intramural fibroids.

Outcome	Number of studies/substudies	Relative risk	95% confidence interval	Significance
<b>A. All studies</b>				
Clinical pregnancy rate	12	0.810	0.696-0.941	$P=.006$
Implantation rate	7	0.684	0.587-0.796	$P<.001$
Ongoing pregnancy/live birth rate	8	0.703	0.583-0.848	$P<.001$
Spontaneous abortion rate	8	1.747	1.226-2.489	$P=.002$
Preterm delivery rate	1	6.000	0.309-116.606	Not significant
<b>B. Prospective studies</b>				
Clinical pregnancy rate	3	0.708	0.437-1.146	Not significant
Implantation rate	2	0.552	0.391-0.781	$P=.001$
Ongoing pregnancy/live birth rate	2	0.465	0.291-0.744	$P=.019$
Spontaneous abortion rate	2	2.384	1.110-5.122	$P=.002$
Preterm delivery rate	0	—	—	—
<b>C. Studies using hysteroscopy in all subjects</b>				
Clinical pregnancy rate	2	0.845	0.666-1.071	Not significant
Implantation rate	1	0.714	0.547-0.931	$P=0.013$
Ongoing pregnancy/live birth rate	2	0.733	0.383-1.405	Not significant
Spontaneous abortion rate	2	1.215	0.391-3.774	Not significant
Preterm delivery rate	1	6.000	0.309-116.606	Not significant

Prints. Fibroids and infertility. *Reprod Steril* 2009.

## Impact on fertility



SYMPOSIUM: REPRODUCTIVE SURGERY REVIEW

### Is another meta-analysis on the effects of intramural fibroids on reproductive outcomes needed?

Mostafa Metwally <sup>a,\*</sup>, Cynthia M Farquhar <sup>b</sup>, Tin Chiu Li <sup>c</sup>

Concern: Heterogeneity & Quality of studies included  
Re-analysis: Include only high-quality studies

Third meta-analysis

### IM fibroid & miscarriage rate

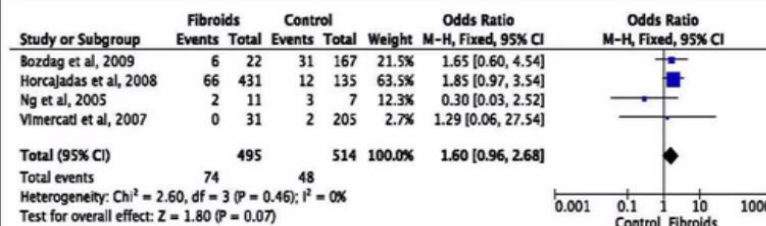


Figure 4 The effect of presence of intramural fibroids on the miscarriage rate after assisted conception.

Third meta-analysis

### IM fibroid & LB rate

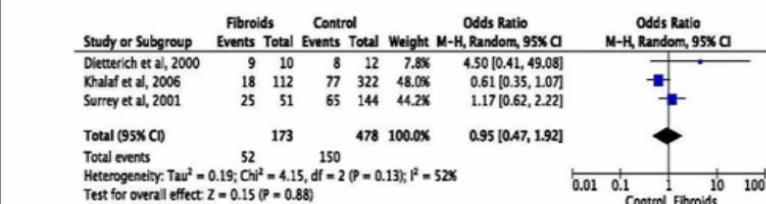


Figure 2 The effect of presence of intramural fibroids on the live birth rate after assisted conception.

Third meta-analysis

### The effect of intramural fibroids without uterine cavity involvement on the outcome of IVF treatment: a systematic review and meta-analysis

Sesh Kamal Sunkara<sup>1</sup>, Mohammed Khairy, Tarek El-Toukhy, Yacoub Khalaf, and Arri Coomarasamy

Human Reproduction, Vol.25, No.2 pp. 418-429, 2010



Figure 3 Forest plot of studies of non-cavity-distorting intramural fibroids birth rates.

Second meta-analysis





# “Confounders factors”

Tumor volume

Definition of  
intramural myomas

Number of myomas

Impact on fertility of  
intramural myomas

Genetic heterogeneity

Thickness of  
intervening  
myometrium

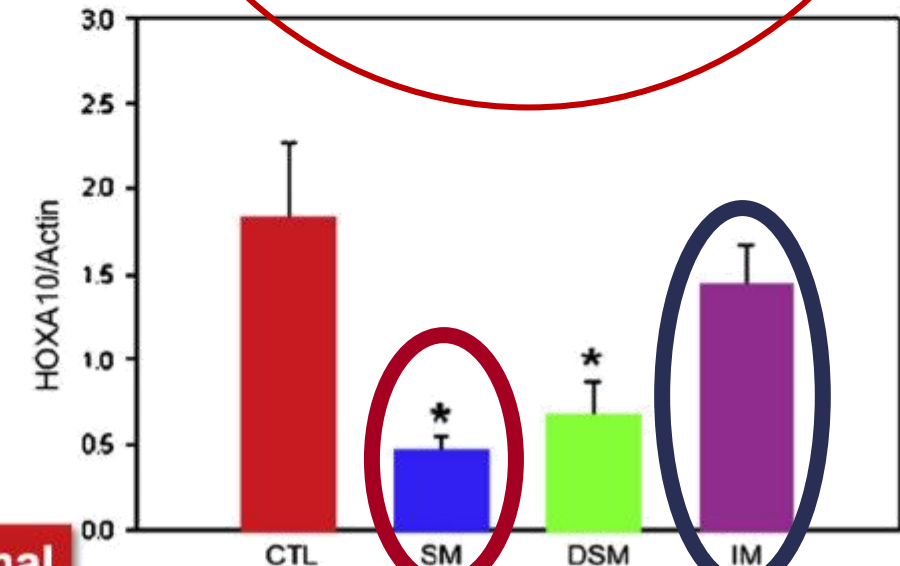
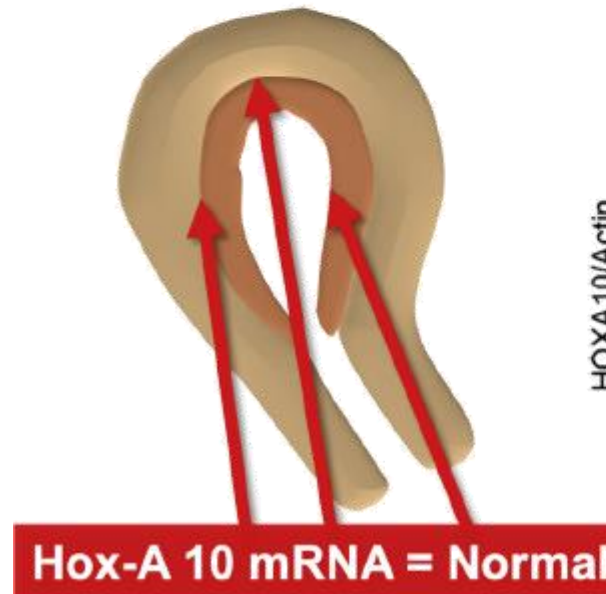
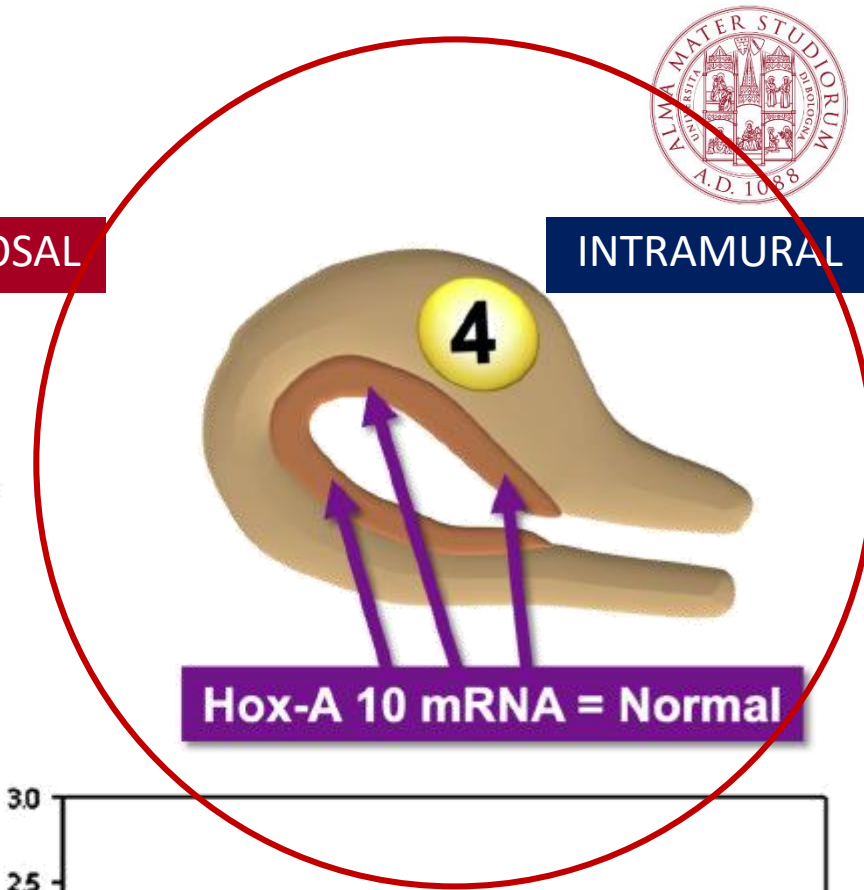
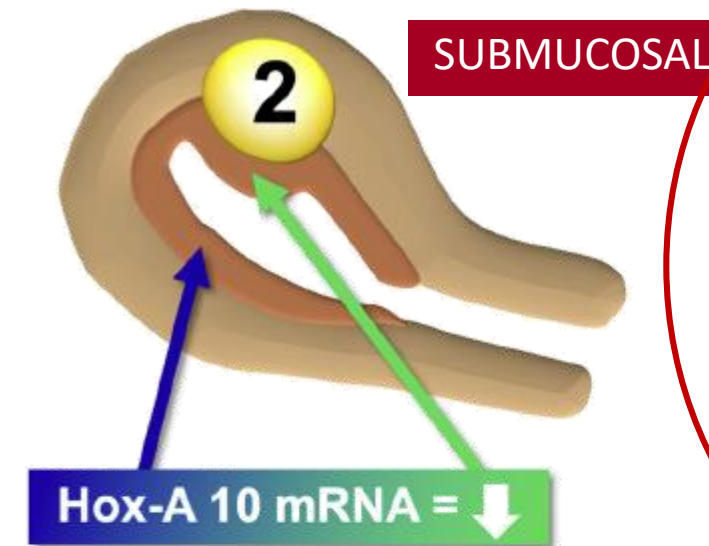
Low grade evidence, few studies

# Impact on fertility

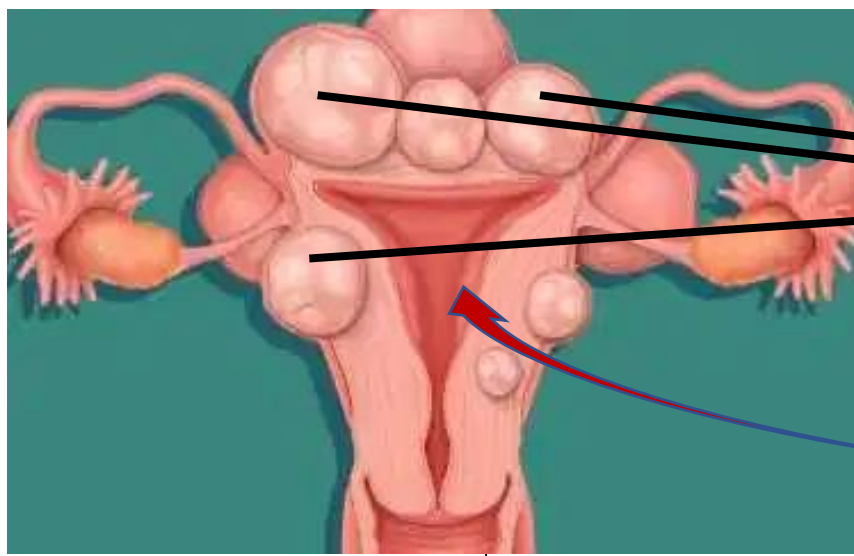
Endometrial Hox-A10 messenger RNA expression



Involved in decidualization and implantation



Adapted from Rackow et al Fertil Steril 2010



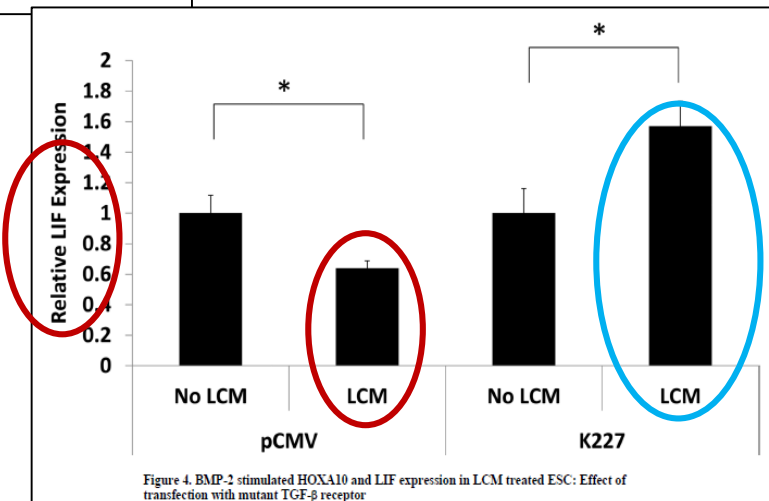
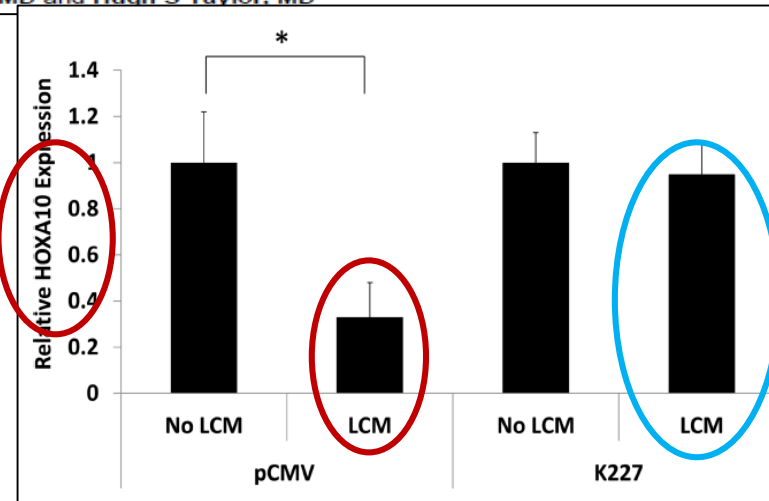
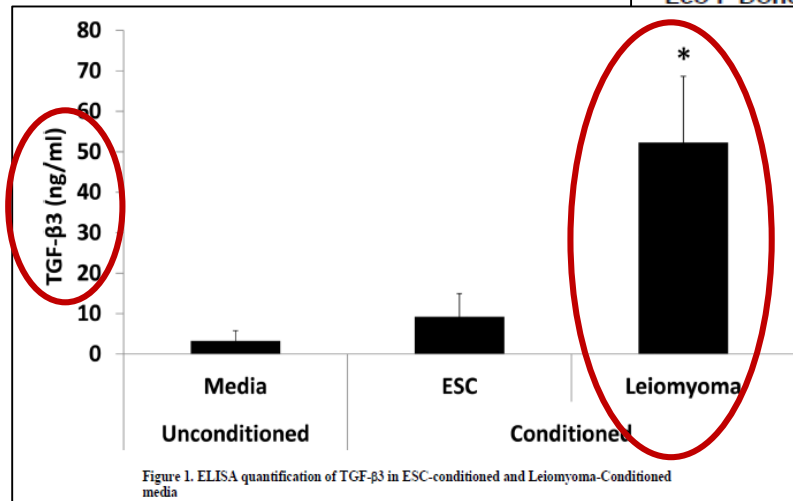
>TGF-Beta

Bone morphogenetic protein  
type 1 and 2 receptors

*Fertil Steril.* 2015 March ; 103(3): 845–852. doi:10.1016/j.fertnstert.2014.12.099.

### Leiomyoma-Derived TGF- $\beta$ Impairs BMP-2 Mediated Endometrial Receptivity

Leo F Doherty, MD and Hugh S Taylor, MD



### Conclusions—

- Leiomyoma derived TGF- $\beta$  was necessary and sufficient to alter endometrial BMP-2 responsiveness.
- Blockade of TGF- $\beta$  prevents repression of BMP-2 receptors and restores BMP-2 stimulated expression of HOXA10 and LIF.
- Blockade of TGF signaling is a potential strategy to improve infertility and pregnancy loss associated with uterine leiomyoma.

## Effect of large intramural fibroids (>5 cm)

Hart R et al Hum Reprod 2001 16: 2411

### IVF Outcome

Implantation rate reduced from 20.2 to 11.9 % (p=0.018)

Pregnancy rate reduced from 34.1 % to 23.3 % (p=0.016)

Ongoing PR reduced from 28.3 to 15.1 % (p=0.003)

Large intramural myoma negatively affects  
outcome after IVF

## Impact on fertility

### Fibroids not encroaching the endometrial cavity and IVF success rate: a prospective study

Edgardo Somigliana<sup>1,\*</sup>, Silvia De Benedictis<sup>1,2</sup>, Paolo Vercellini<sup>1,2</sup>,  
Anna Elisa Nicolosi<sup>1</sup>, Laura Benaglia<sup>1,2</sup>, Claudia Scarduelli<sup>1</sup>,  
Guido Ragni<sup>1</sup>, and Luigi Fedele<sup>1,2</sup>

Human Reproduction, Vol.26, No.4 pp. 834-839, 2011

119 cases and 119 controls  
In asymptomatic patients selected for IVF,  
small fibroids (<5cm) not encroaching the  
endometrial cavity did not affect clinical  
pregnancy and LB rates







# Impact on fertility

## Effect of type 3 intramural fibroids on in vitro fertilization–intracytoplasmic sperm injection outcomes: a retrospective cohort study

Fertility and Sterility®  
Copyright ©2018 Amer

Lei Yan, M.D., Ph.D., Qian Yu, M.D., Ya-nan Zhang, M.D., Zizhen Guo, M.D., Zhongyuan Li, M.D., Jinlei Niu, M.D., and Jinlong Ma, M.D., Ph.D.

### INTRAMURAL

RETROSPECTIVE STUDY  
151 patients with FIGO 3 myomas vs  
453 matched controls

In vitro fertilization–intracytoplasmic sperm injection outcomes in the case and the control groups.

Outcome	Case	Control	P value	OR (95% CI)	P value <sup>a</sup>
Cancellation	33/151 (21.8)	69/453 (15.5)	.079	1.32 (0.81–2.17)	.267
Biochemical pregnancy	44/151 (29.1)	233/453 (51.4)	<.001	0.43 (0.29–0.64)	<.001
Clinical miscarriage	10/42 (23.8)	44/199 (22.1)	.839		
Clinical pregnancy	42/151 (27.8)	199/453 (43.9)	.001	0.53 (0.35–0.80)	.003
Implantation	55/242 (22.7)	264/768 (34.4)	.001		
Preterm delivery	3/151 (2.0)	15/453 (3.3)	.582		
Live birth	32/151 (21.2)	156/453 (34.4)	.002	0.57 (0.36–0.89)	.013
Singleton	25/151 (16.6)	116/453 (25.6)	.026	0.66 (0.41–1.07)	.093
Twin	7/151 (4.6)	40/453 (8.8)	.114	0.47 (0.20–1.12)	.09

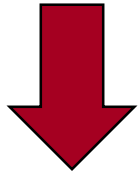
Note: Data presented as n (%) and odds ratio (95% confidence interval). CI = confidence interval; OR = odds ratio.

<sup>a</sup> Logistic regression analysis was conducted by adjusting for use of “other protocol” of ovary stimulation.

Type 3 fibroids exert a negative impact on the rates of implantation, clinical pregnancy, and livebirth in patients undergoing IVF-ICSI, but do not significantly increase the clinical miscarriage rate, in particular for diameter > 2 cm

# Impact on fertility

SUBMUCOSAL



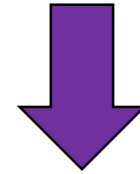
Definite impact on fertility

INTRAMURAL



Controversial impact on fertility

SUBSerosal



No impact on fertility

TREATMENT ???

# Surgical approach to Uterine Myomas in women with reproductive expectancies

- Myomas and fertility.
- Does myomectomy improve fertility outcomes?
- Surgical technique?
- Strategies to improve surgical outcomes
- And after surgery? Pregnancy after myomectomy



# Does myomectomy improve fertility outcomes?

## Fibroids and infertility: an updated systematic review of the evidence

2009

Elizabeth A. Pritts, M.D.,<sup>a</sup> William H. Parker, M.D.,<sup>b</sup> and David L. Olive, M.D.<sup>a</sup>

Effect of myomectomy on fertility: submucosal fibroids.				
Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
<b>A. Controls: fibroids in situ (no myomectomy)</b>				
Clinical pregnancy rate	2	2.034	1.081–3.826	$P = .028$
Implantation rate	0	—	—	—
Ongoing pregnancy/live birth rate	1	2.654	0.920–7.658	Not significant
Spontaneous abortion rate	1	0.771	0.359–1.658	Not significant
Preterm delivery rate	0	—	—	—
<b>B. Controls: infertile women with no fibroids</b>				
Clinical pregnancy rate	2	1.545	0.998–2.391	Not significant
Implantation rate	2	1.116	0.906–1.373	Not significant
Ongoing pregnancy/live birth rate	3	1.128	0.959–1.326	Not significant
Spontaneous abortion rate	2	1.241	0.475–3.242	Not significant
Preterm delivery rate	0	—	—	—

*Pritts. Fibroids and infertility. Fertil Steril 2009.*

Fertility outcomes are decreased in women with submucosal fibroids, and removal seems to confer benefit

Effect of myomectomy on fertility: intramural fibroids (fibroids in situ controls).				
Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	2	3.765	0.470–30.136	Not significant
Implantation rate	0	—	—	—
Ongoing pregnancy/live birth rate	1	1.671	0.750–3.723	Not significant
Spontaneous abortion rate	1	0.758	0.296–1.943	Not significant
Preterm delivery rate	0	—	—	—

*Pritts. Fibroids and infertility. Fertil Steril 2009.*

• In patients with intramural fibroids, myomectomy seems no have influence in reproductive outcomes



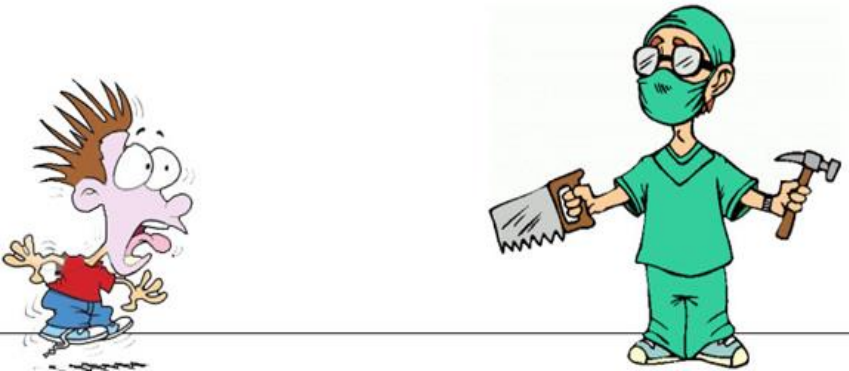
## The Management of Uterine Fibroids in Women With Otherwise Unexplained Infertility

### Recommendations

- In women with otherwise unexplained infertility, **submucosal fibroids should be removed** in order to improve conception and pregnancy rates. (II-2)
- **Removal of subserosal fibroids is not recommended.** (III-D)
- There is fair evidence to recommend against myomectomy in women with **intramural fibroids** (hysteroscopically confirmed intact endometrium) and otherwise unexplained infertility, regardless of the size of the fibroids. (II-2D) If the patient has no other options, **the benefits of myomectomy should be weighed against the risks, and management of intramural fibroids should be individualized.** (III-C)



# Therapy



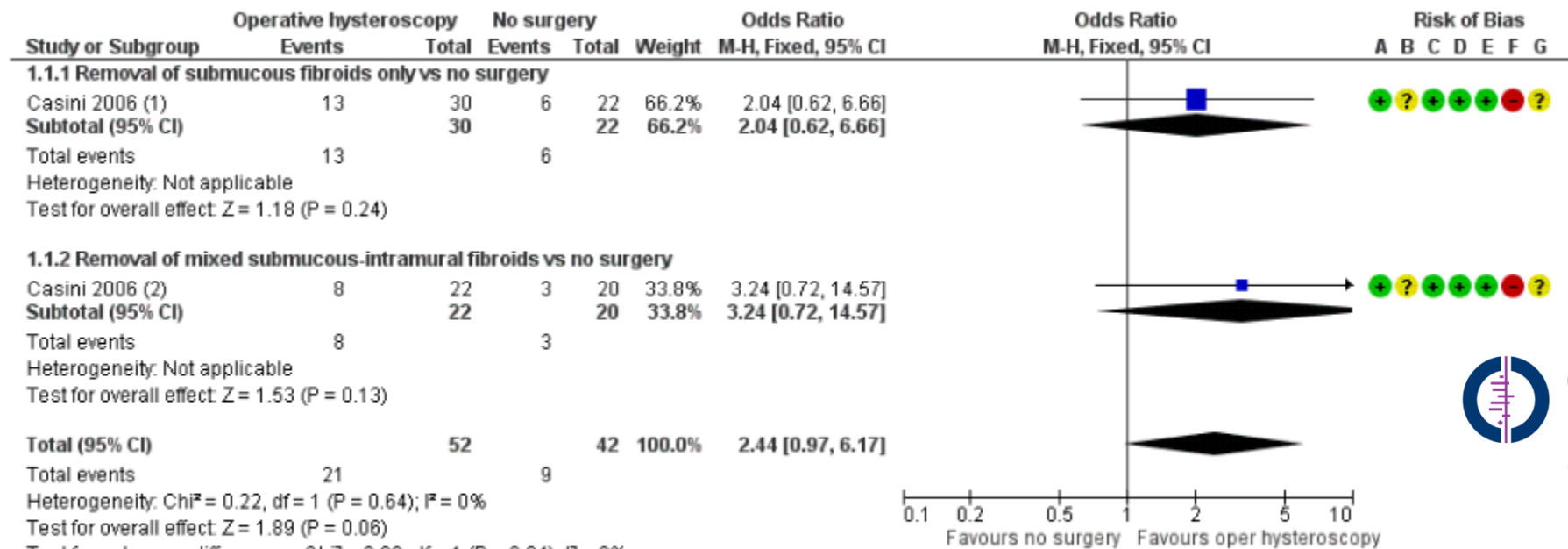
# Treatment

## SUBMUCOSAL

### Hysteroscopy for treating subfertility associated with suspected major uterine cavity abnormalities (Review)

Bosteels J, van Wessel S, Weyers S, Broekmans FJ, D'Hooghe TM, Bongers MY, Mol BWJ

**Figure 4. Forest plot of comparison: I Hysteroscopic myomectomy vs no surgery in women with unexplained subfertility and submucous fibroids. Outcome: I.1 Clinical pregnancy per woman randomised.**

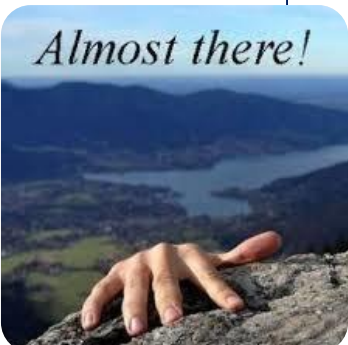


#### Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

**Footnotes**  
(1) The intervention was the hysteroscopic removal of fibroids. The comparison arm was no...  
(2) The intervention was the hysteroscopic removal of fibroids. The comparison arm was no...

p 0.06



# Laparoscopic vs open myomectomy

## Surgical treatment of fibroids for subfertility (Review)

Metwally M, Cheong YC, Horne AW

2012



Clinical pregnancy rate

Miscarriage rate

**NO**  
DIFFERENCE

Cesarean section

Figure 5. Forest plot of comparison: 2 Open versus laparoscopic myomectomy, outcome: 2.2 Clinical pregnancy rate.

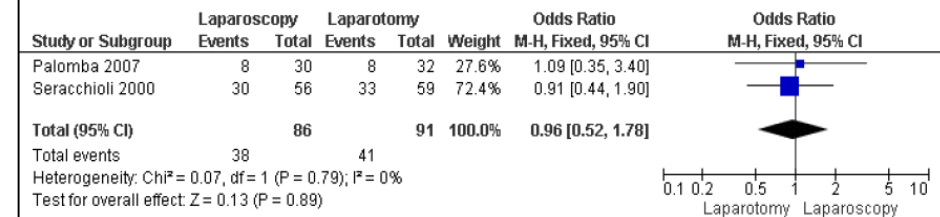


Figure 6. Forest plot of comparison: 2 Open versus laparoscopic myomectomy, outcome: 2.4 Miscarriage rate.

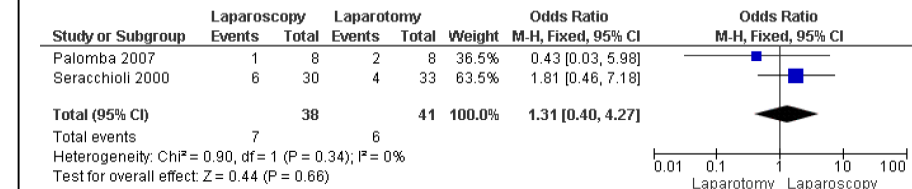


Figure 4. Forest plot of comparison: 2 Open versus laparoscopic myomectomy, outcome: 2.1 Live birth rate.

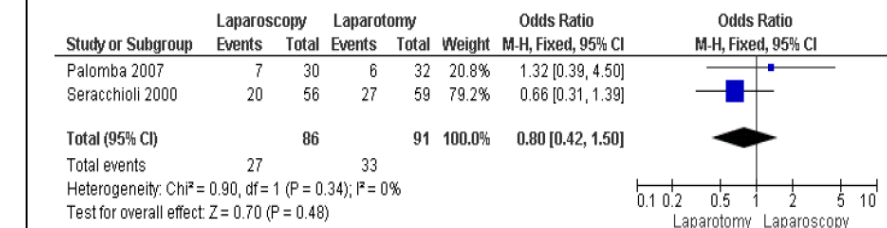
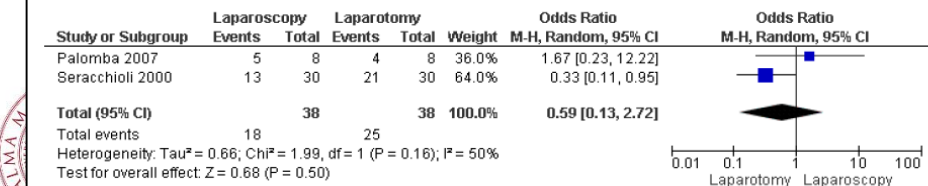


Figure 7. Forest plot of comparison: 2 Open versus laparoscopic myomectomy, outcome: 2.5 Caesarean section rate.







**Cochrane**  
**Library**

Cochrane Database of Systematic Reviews

2014

**Minimally invasive surgical techniques versus open myomectomy for uterine fibroids (Review)**

Bhave Chittawar P, Franik S, Pouwer AW, Farquhar C

**MYOMECTOMY:  
LAPAROSCOPY vs. OPEN**

**9 trials**

**808 women**

## Laparoscopy vs. open:

- < pain at 6-48h after surgery
- < postoperative complications
- < hospitalization times

**Similar recurrence rates(OR 1.12, 95% CI 0.63 to 1.99).**



ELSEVIER

www.sciencedirect.com  
www.rbmonline.com



REVIEW

**Safety and efficacy of the minilaparotomy for myomectomy: a systematic review and meta-analysis of randomized and non-randomized controlled trials**



Stefano Palomba <sup>a,\*</sup>, Eleonora Fornaciari <sup>a</sup>, Angela Falbo <sup>a</sup>,  
Giovanni Battista La Sala <sup>a,b</sup>

RBO, 2015

**Myomectomy:  
LAPAROSCOPY vs. MINI-LAP vs. LAP**

Surgical time	<u>Mini-lap</u> > lap > lps
HB level	<u>Mini-lap</u> = <u>lps</u> > lap
Ileus postop	<u>Lps</u> > mini-lap > lap
Hospitaliz.	<u>mini-lap</u> = <u>lps</u> > lap

## The Management of Uterine Fibroids in Women With Otherwise Unexplained Infertility

### Summary Statement

- In the infertile population, cumulative pregnancy rates by the laparoscopic and minilaparotomy approaches are similar, but **the laparoscopic approach is associated with a quicker recovery, less postoperative pain, and less febrile morbidity.** (II-2)

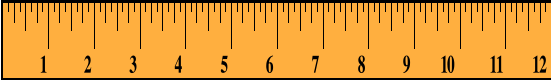
### Recommendation

- Widespread use of **the laparoscopic approach** to myomectomy may be **limited by the technical difficulty of this procedure.** Patient selection should be individualized based on the number, size, and location of uterine fibroids and the skill of the surgeon. (III-A)

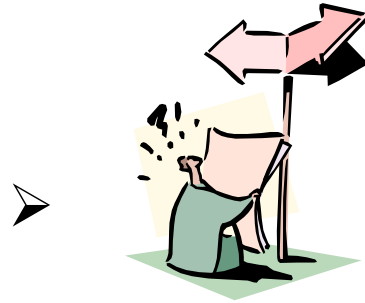
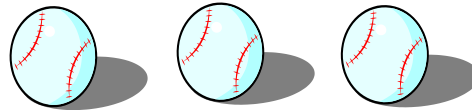


# ***PATIENT SELECTION LIMITS***



➤  **Volume**

➤ **Number**



**Location**

➤ **Surgical experience**



**Surgical risks**



**Operating time**



# Surgical approach to Uterine Myomas in women with reproductive expectancies

- Myomas and fertility.
- Does myomectomy improve fertility outcomes
- Surgical technique?
- Strategies to improve surgical outcomes
- And after surgery? Pregnancy after myomectomy



# Before Surgery

## MEDICAL THERAPY

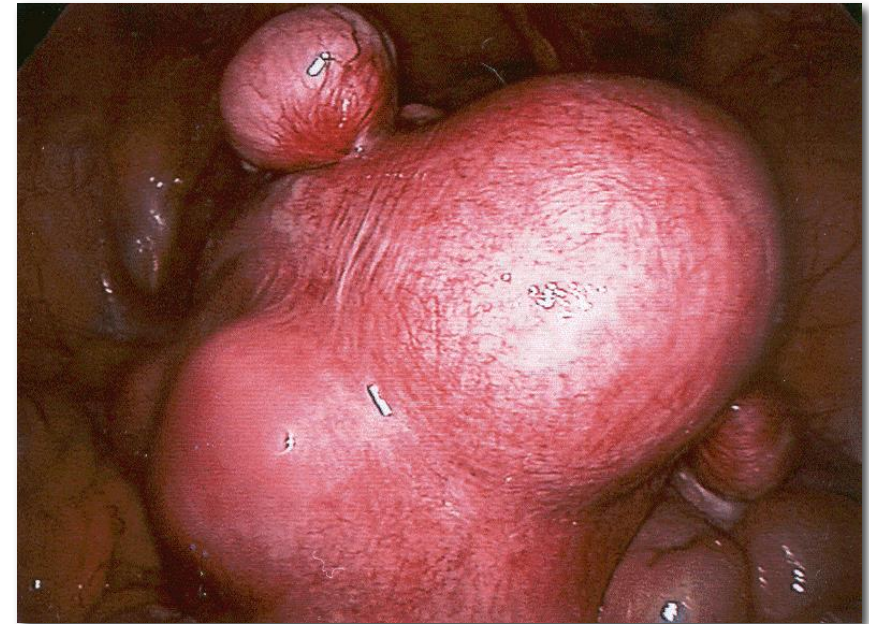
- stop bleeding
- correct anemia
- improve the quality of life
- decrease the volume of the leiomyomas.
- The surgical approach can be changed if the uterine volume decreases significantly.
- Two medical therapies have proven to be effective in this indication:
- GnRHa and SPRM (ulipristal acetate).



# During Surgery

## PERIOPERATIVE BLOOD-SAVING TECHNIQUES

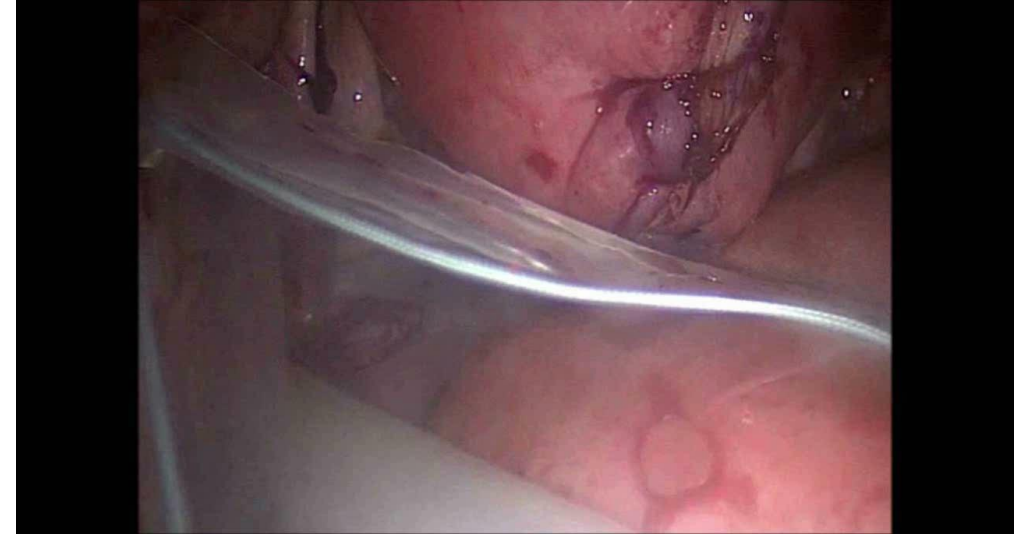
- pericervical “tourniquet” technique
- preoperative embolization
- preventive uterine arteries occlusion
- use uterotonic or vasoconstrictive agents: oxytocine, misoprostol, or sulprostone
- intrauterine injection of vasopressin or epinephrine + bupivacaine



# During Surgery

## Alternatives and Other Approaches to Morcellation

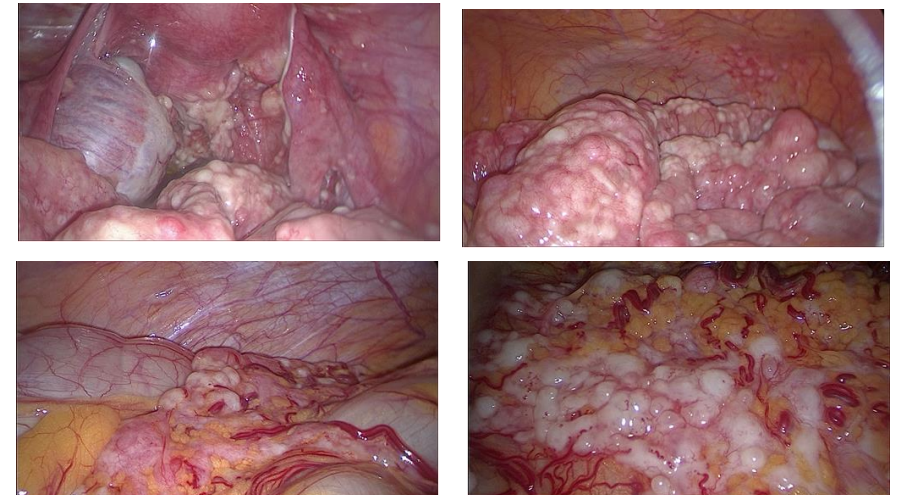
- For women undergoing myomectomy, the American College of Obstetricians and Gynecologists recommends a minimally invasive approach whenever feasible.
- **Alternative to power morcellation**
- morcellation through suprapubic or umbilical incisions with containment bags
- hand-assisted morcellation through a mini-laparotomy
- vaginal morcellation



Not only malignancies....

**Fertility  
and Sterility.**

Video of the month  
(June 2019)



# Surgical approach to Uterine Myomas in women with reproductive expectancies

- Myomas and fertility.
- Does myomectomy improve fertility outcomes
- Surgical technique?
- Strategies to improve surgical outcomes
- And after surgery? Pregnancy after myomectomy





# And after surgery?



Actually there is no consensus about...



Time to wait for pregnancy

About 4-6 months for IM myomas

Mode of delivery

Not always cesarean section!!!

Risk of uterine rupture

< 1% often III trimester but before labor

# Treatment

## Obstetric and delivery outcome of pregnancies achieved after laparoscopic myomectomy

Renato Seracchioli, M.D., Linda Manuzzi, M.D., Federico Vianello, M.D., Beatrice Gualerzi, M.D., Luca Savelli, M.D., Roberto Paradisi, M.D., and Stefano Venturoli, M.D.

**TABLE 2**

### Outcome of the 158 pregnancies after laparoscopic myomectomy.

	n	%
Number of pregnancies	158	100.0
Spontaneous abortion	43	27.2
Voluntary abortion	1	0.6
Extra uterine pregnancies	4	2.6
Endo uterine fetal death	1	0.6
Deliveries	106	67.0
Pregnancies in progress	3	1.8

Seracchioli. Obstetric and delivery outcome after LM. Fertil Steril 2006.

**TABLE 4**

### Main features of 106 deliveries after laparoscopic myomectomy.

	n	%
Mode of delivery		
Spontaneous delivery	27	25.5
Operative delivery	0	0
Elective caesarean section	62	58.5
Cesarean section on emergency	17	16.0
Fetal distress	8	
Premature rupture of membranes	2	
Dynamic dystocia	6	
Gestational hypertension	1	
Perinatal outcome		
Gestational age (wk)	38.20 ± 1.28	
Premature delivery <36 wk	2	2
Ended delivery >36 wk	104	98.1
Intrauterine fetal death	1	0.9
Obstetric complications		
Uterine rupture	0	0
Postpartum hemorrhage	0	0
Hysterectomy (elective postcesarean)	1	0.9

Seracchioli. Obstetric and delivery outcome after LM. Fertil Steril 2006.

LPS myomectomy performed by an expert surgeon can restore reproductive capacity, allowing patients to have a successful pregnancy

## National survey of uterine rupture in Japan: Annual report of Perinatology Committee, Japan Society of Obstetrics and Gynecology, 2018

Shintaro Makino<sup>1,2</sup>, Satoru Takeda<sup>1,2</sup>, Eiji Kondoh<sup>1,3</sup>, Kenta Kawai<sup>1,4</sup>, Jun Takeda<sup>2</sup>, Shigeki Matsubara<sup>1,5</sup>, Atsuo Itakura<sup>1,2</sup>, Haruhiko Sago<sup>1,6</sup>, Shinji Tanigaki<sup>1,7</sup>, Mamoru Tanaka<sup>1,8</sup>, Tomoaki Ikeda<sup>1,9</sup> and Naohiro Kanayama<sup>1,4</sup>

**Table 1** Details of uterine rupture during pregnancy

Surgery	n (%)	Median (weeks)	Hysterectomy, n (%)	Apgar score ≤ 6, n (%)	UmApH ≤ 7.1, n (%)	UmABE ≤ 12, n (%)	Cerebral palsy, n (%)	Neonatal death, n (%)
Cesarean section	74 (48.7)	37.0	5 (6.8)	8 (10.8)	8 (10.8)	5 (6.8)	0	4 (5.4)
Myomectomy								
Abdominal	7 (4.6)	32.3	0	0	0	0	0	2 (28.6)
Laparoscopic	17 (11.2)	32.5	3 (17.6)	3 (17.6)	3 (17.6)	1 (5.9)	0	3 (17.6)
Adenomyomectomy								
Abdominal	3 (2.0)	30.0	2 (66.7)	0	0	0	0	0
Laparoscopic	4 (2.6)	32.0	1 (25.0)	—	—	—	2 (50.0)	2 (50.0)
Unscarred	40 (26.3)	39.0	21 (52.5)	10 (25)	10 (25)	4 (10)	5 (12.5)	7 (17.5)

UmABE, umbilical arterial blood base excess; UmApH, umbilical arterial blood pH.

- 152 cases (in 5 years) of uterine rupture with an incidence rate of 0.015%.
- week of occurrence of uterine ruptures  
unscarred 39.0 weeks, cesarean section 37.0 weeks, myomectomy 32 weeks, adenomyomectomy 30–32 weeks.

## Trial of labor after myomectomy and uterine rupture: a systematic review

ZITA GAMBACORTI-PASSERINI<sup>1</sup>, ALEXIS C. GIMOVSKY<sup>2</sup>, ANNA LOCATELLI<sup>1</sup> & VINCENZO BERGHELLA<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, University of Milan Bicocca, Milan, Italy, and <sup>2</sup>Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Sidney Kimmel College of Medicine, Thomas Jefferson University, Philadelphia, PA, USA

Z. Gambacorti-Passerini et al.

Review of uterine rupture during trial of labor after myomectomy

**Table 2.** Rate of uterine rupture in eleven studies that reported detailed data about trial of labor after myomectomy.

Author	Year	Pregnancies	Pregnancy after myomectomy	Deliveries (≥24 weeks)	UR before TOLAM	TOLAM	UR in TOLAM
Dubuisson (16)	2000	145	All subsequent	100	2/28	72/100	0/72
Seracchioli (18)	2000	63	Not specified	47	0/25	22/47	0/22
Dessolle (19)	2001	44	All subsequent	34	0/4	30/34	0/30
Seracchioli (24)	2006	158	All subsequent	106	0/65	41/106	0/41
Palomba (26)	2007	62	1st pregnancy only	54	0/19	35/54	0/35
Makino (27)	2008	109	Not specified	109	0/45	64/109	0/64
Kelly (28)	2008	93	All subsequent	93	1/38	55/93	0/55
Kumakiri (8)	2008	221	1st pregnancy only	111	0/37	74/111	0/74
Lonnerfors (29)	2011	18	All subsequent	10	0/4	6/10	0/6
Kim (31)	2013	66	Not specified	53	0/47	6/53	0/6
Bernardi (32)	2014	55	All subsequent	39	2/18	21/39	2/21
Total		1034		756	<b>1.52%</b> (5/330)	<b>56.35%</b> (426/756)	<b>0.47%</b> (2/426)

TOLAM, Trial of labor after myomectomy; UR, uterine rupture.

# Leiomyomatous uterus and preterm birth: an exposed/unexposed monocentric cohort study

Aude Girault, MD; Camille Le Ray, MD, PhD; Charles Chapron, MD, PhD; François Goffinet, MD, PhD; Louis Marcellin, MD, PhD

OCTOBER 2018 American Journal of Obstetrics & Gynecology 410.e2



ALMA MATER STUDIORUM – UNIVERSITÀ DI BOLOGNA - ITALY



TABLE 2

Comparison of pregnancy outcomes and characteristics of delivery between groups of leiomyomatous uterus and nonleiomyomatous uterus, n = 19,866

Pregnancy outcomes and characteristics of delivery	Leiomyomatous uterus n = 301	Nonleiomyomatous uterus n = 19,565	P
Medical pathology during pregnancy, n (%)			
Gestational hypertension	21 (7.0)	288 (1.5)	<.001
Gestational diabetes	53 (17.6)	1477 (7.6)	<.001
Other significant medical pathology	0 (0)	4743 (24.4)	NA
Obstetrical pathology during pregnancy, n (%)			
PPROM ± TPD	14 (4.7)	845 (4.3)	.8
Preeclampsia	19 (6.3)	480 (2.4)	<.001
Placenta previa	15 (5.0)	146 (0.8)	<.001
Gestational age at rupture of membrane, WG, mean ± SD	36.7 ± 3.0	37.0 ± 9.1	.59
At least 1 hospitalization during pregnancy, n (%)	116 (38.5)	5721 (29.2)	<.001
Type of onset of labor, n (%)			
Spontaneous	138 (45.9)	13,200 (67.5)	<.001
Induction	48 (15.9)	4126 (21.1)	
Cesarean before labor	115 (38.2)	2153 (11.0)	
Delivery <37 WG, n (%)	36 (12.0)	1650 (8.4)	.03
Delivery <34 WG, n (%)	23 (7.6)	811 (4.1)	.003
Type of preterm birth, n (%)			
Spontaneous birth <37 WG	15 (5.0)	820 (4.2)	
Induced preterm birth <37 WG	21 (7.0)	830 (4.2)	
Fetal presentation, n (%)			
Cephalic	255 (84.7)	18,369 (93.9)	<.001
Breech	35 (11.6)	928 (4.7)	
Transverse lie	11 (3.7)	96 (0.5)	
Face or brow	0 (0.0)	33 (0.2)	
Type of delivery, n (%)			
Spontaneous	122 (40.5)	12,952 (66.2)	<.001
Operative vaginal	19 (6.3)	1961 (10.0)	
Cesarean	160 (53.2)	4644 (23.8)	
PPH, n (%)	47 (15.6)	1077 (5.5)	<.001
Peripartum transfusion, n (%)	20 (6.6)	89 (0.5)	<.001

NA, not applicable; PPH, postpartum hemorrhage; PPRM, preterm premature rupture of membranes; TPD, threatened preterm delivery; WG, weeks of gestation.

Girault et al. Leiomyomatous uterus and preterm birth. Am J Obstet Gynecol 2018.



# There must always be an indication for surgery

The first great error in surgery is to operate unnecessarily

The second, to undertake an operation for which the surgeon is not sufficiently skilled technically

- Max Thorek, 1880-1960



THANK YOU



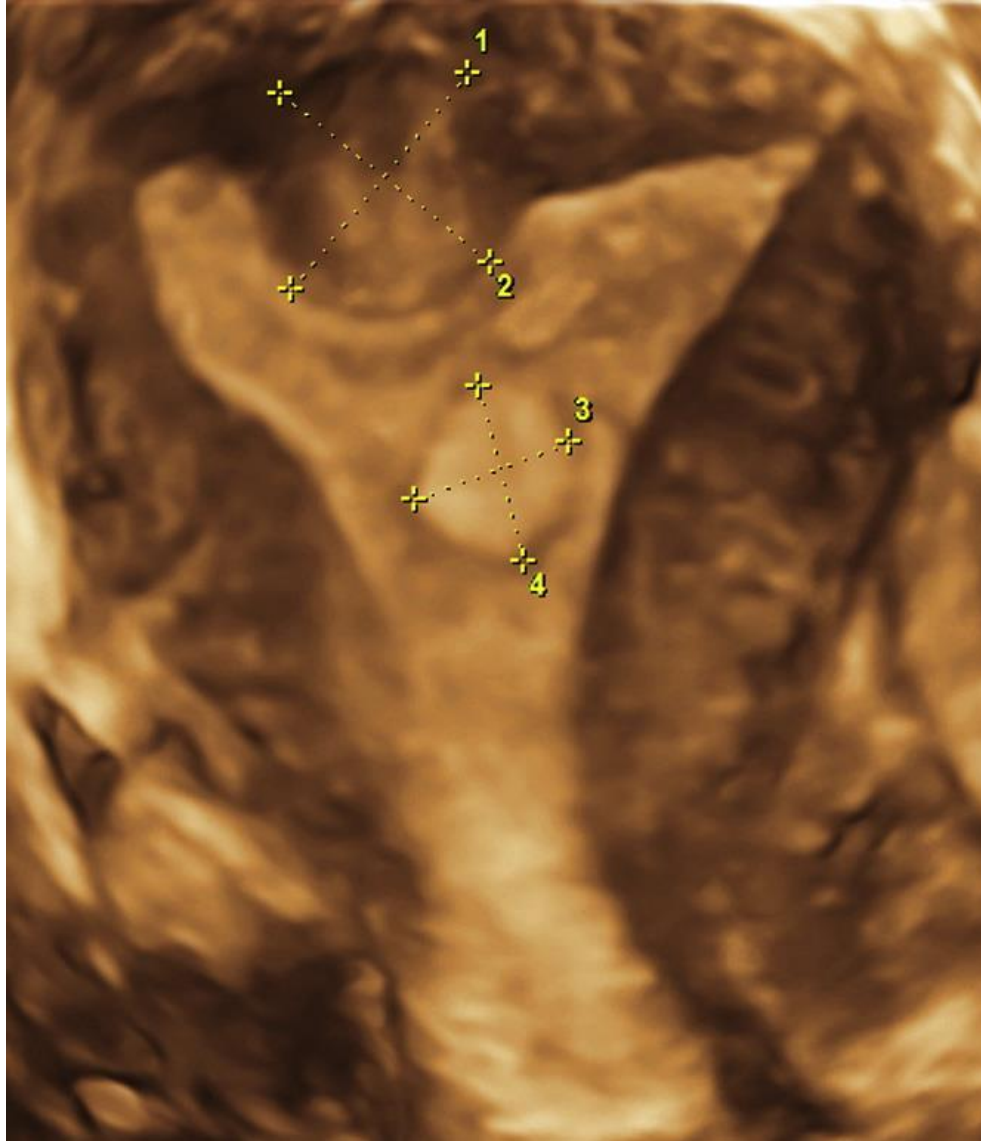


- Endometrial receptivity and embryo implantation
- Fibroids and fertility
- Which fibroids may affect fertility?
- Which fibroids have to be removed?
- How fibroids have to be removed? Which surgical technique?
- Different surgical strategies
- And after surgery? Pregnancy after myomectomy
- Variables



# Impact on fertility

## SUBMUCOSAL



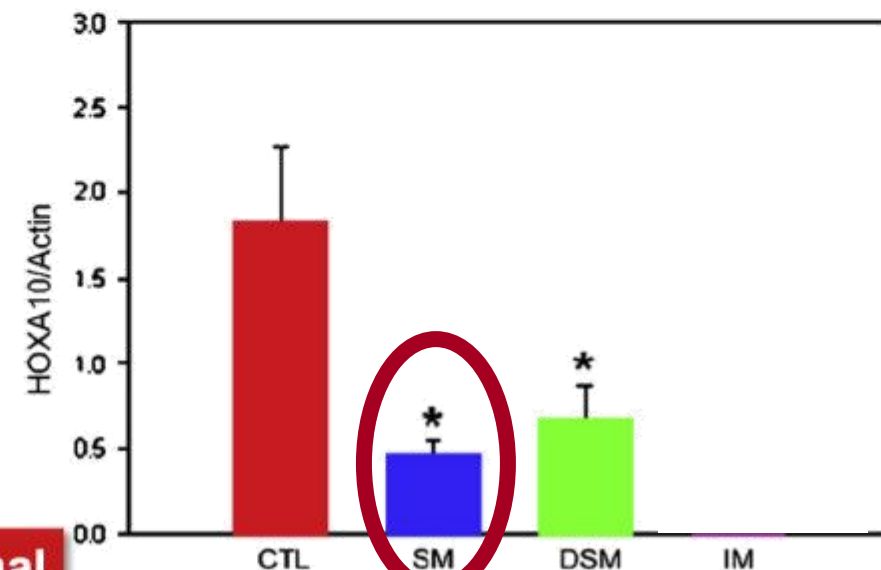
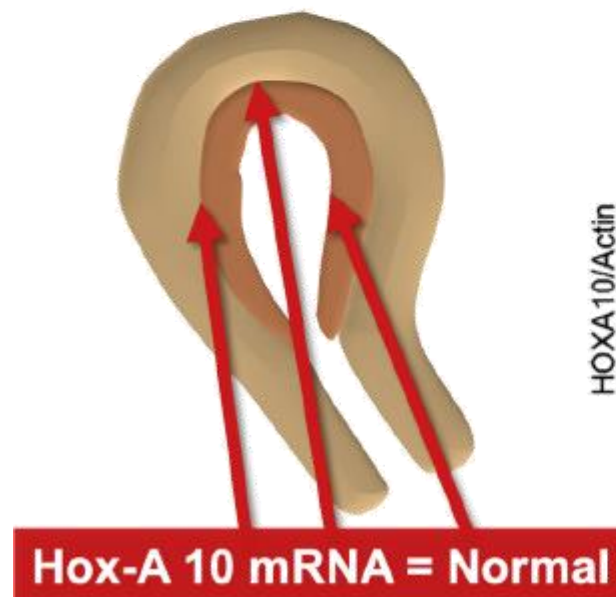
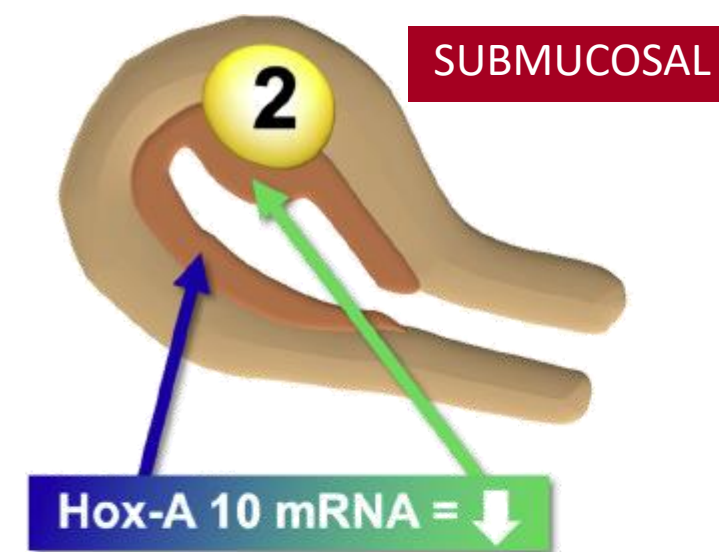
- ✓ Uterine cavity distortion
- ✓ Abnormally increased uterine contractility
- ✓ Abnormal vascularization
- ✓ Disturbances in endometrial cytokine expression
- ✓ Chronic endometrial inflammation
- ✓ **Difficult implantation**

# Impact on fertility

Endometrial Hox-A10  
messenger RNA  
expression



Involved in  
decidualization and  
implantation



Adapted from Rackow et al Fertil Steril 2010



In case of symptomatic uterine leiomyomas, medical, surgical, or radiological therapies may

be chosen depending on a range of criteria:

- the age,
- the desire to become pregnant,
- the desire to preserve the uterus,
- the number, the size and the location of the leiomyomas,
- the main symptom,
- the comorbidities,
- the anticipated surgical difficulties (multiple prior surgeries, multiple myomectomies),
- the level of experience of the therapist.

# Miomectomy e PMA

## Myomas, Pregnancy Outcome, and *In Vitro* Fertilization

CARLO BULLETTI,<sup>a</sup> DOMINIQUE DE ZIEGLER,<sup>b</sup> PAOLO LEVI SETTI,<sup>c</sup>  
ETTORE CICINELLI,<sup>d</sup> VALERIA POLLI,<sup>a</sup> AND MARCO STEFANETTI<sup>a</sup>

2004 New York Academy of Sciences.

TABLE 2. Effect of surgical removal of myomas on IVF success rates

	Cumulative pregnancy rate <i>N</i> (% cases)	Delivery rate <i>N</i> (% cases)	Abortion rate <i>N</i> (% pregnancies)
Miomectomy LPS	28 (34)	21 (25)	8 (7)
Miomi NON rimossi	13 (15)	10 (12)	3(4)
	<.05	<.05	Not significant

Miomectomy laparoscopica in pazienti con miomi IM e SS maggiori di 5 cm ha effetti positivi sul cumulative pregnancy rate e sul delivery rate

# Laparoscopic myomectomy: surgical outcomes

European Journal of Obstetrics & Gynecology and Reproductive Biology 145 (2009) 14–21



Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and  
Reproductive Biology

journal homepage: [www.elsevier.com/locate/ejogrb](http://www.elsevier.com/locate/ejogrb)



## Review

### Laparoscopic versus open myomectomy—A meta-analysis of randomized controlled trials

Description of studies.

Author	Year	Grouping LM vs. OM	Follow-up	Mean age (year) LM vs. OM	No. of myomas (n) LM vs. OM	Diameter of the largest one (cm) LM vs. OM	Location
Mais V.	1996	20 vs. 20	6 months	34.3 ± 6.3 vs. 33.8 ± 5.7	–(1–4) vs. –(1–4)	–(3–6) vs. –(3–6)	SS, IM
Seracchioli R.	2000	66 vs. 65	18 months	34 ± 4.11 vs. 33.97 ± 4.79	–	–	SS, IM
Holzer A.	2006	19 vs. 21	52 months	40(31–45) vs. 40(28–49)	2(1–4) vs. 3(1–7)	7(4–10) vs. 5(3–11)	IM
Alessandri F.	2006	74 vs. 74	6 months	37.5 ± 4.5 vs. 38.4 ± 4.9	–	–	SS, IM
Rossetti A.	2001	41 vs. 40	40 months	35 ± 5 vs. 35 ± 3	–(1–7) vs. –(1–7)	–	SS, IM
Stefano	2007	68 vs. 68	12 months	28(21–36) vs. 28(22–38)	1(1–3) vs. 1(1–3)	7.6(5.7–9.8) vs. 7.8(5.5–9.7)	SS, IM

2009

The objective of this study was to determine the better method of myomectomy by comparing laparoscopic and open myomectomy for patients with fibroids with regard to operative parameters and outcomes.

A systematic review was performed on published studies identified by the databases PubMed, EMBASE, the China Biological Medicine Datadase (CBMdisc), Ovid and the Cochrane Library, as well as cross-references. Randomized controlled trials on laparoscopic versus open myomectomy were assessed on operative parameters and outcomes. Six studies and 576 patients were studied. Analysis was performed using the statistical software Review Manager Version 4.2. The data available show that laparoscopic myomectomy was associated with less hemoglobin drop, reduced operative blood loss, more patients fully recuperated at day 15, diminished postoperative pain, and fewer overall complications but longer operation time. However, major complications, pregnancy and recurrence were comparable in the two groups.

The data show that if performed by suitably specialized surgeons in selected patients, laparoscopic myomectomy is a better choice than open surgery.

# Miomectomia Laparoscopica

La miomectomia può determinare importanti complicanze:

- infezioni
- danni a organi interni (intestino, vescica, ureteri)
- sanguinamento e/o emotrasfusione
- aderenze post operatorie
- rischio di rottura d'utero durante la gravidanza e al parto
- aumentato rischio di taglio cesareo

- Minor dolore post operatorio

# Miomectomy Laparoscopica: Outcomes Chirurgici

## Studio italiano sulle complicanze della miomectomy laparoscopica

Tra le più vaste casistiche di casi di miomectomy laparoscopica e la più ampia sulle complicanze

**N° 2050 interventi** di miomectomy laparoscopica (singola o multipla)

**Rischio di complicanze** stimato in relazione a:

- Posizione del mioma: intramurale profondo ( $p < 0.5$ ) o infra-legamentario ( $p < 0.1$ )
- N° miomi  $> 3$  ( $p < 0.001$ )
- Dimensioni → per complicanze maggiori dimensioni  $> 7$  cm ( $p < 0.001$ )

**SE EFFETTUATA DA UN CHIRURGO ESPERTO, la miomectomy LPS può essere considerata una tecnica sicura con un tasso di fallimento estremamente basso e con buoni risultati in termini di outcome riproduttivo**



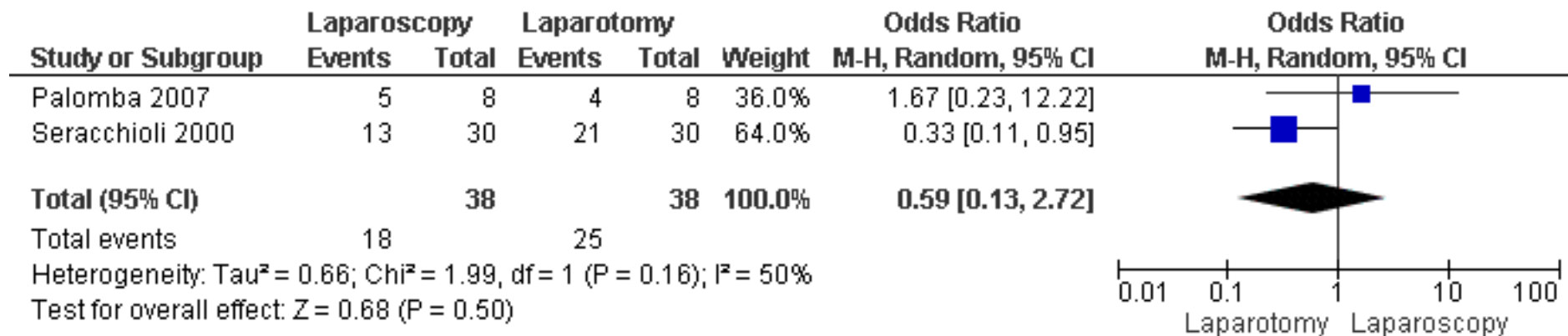
## Surgical treatment of fibroids for subfertility (Review)

Metwally M, Cheong YC, Horne AW

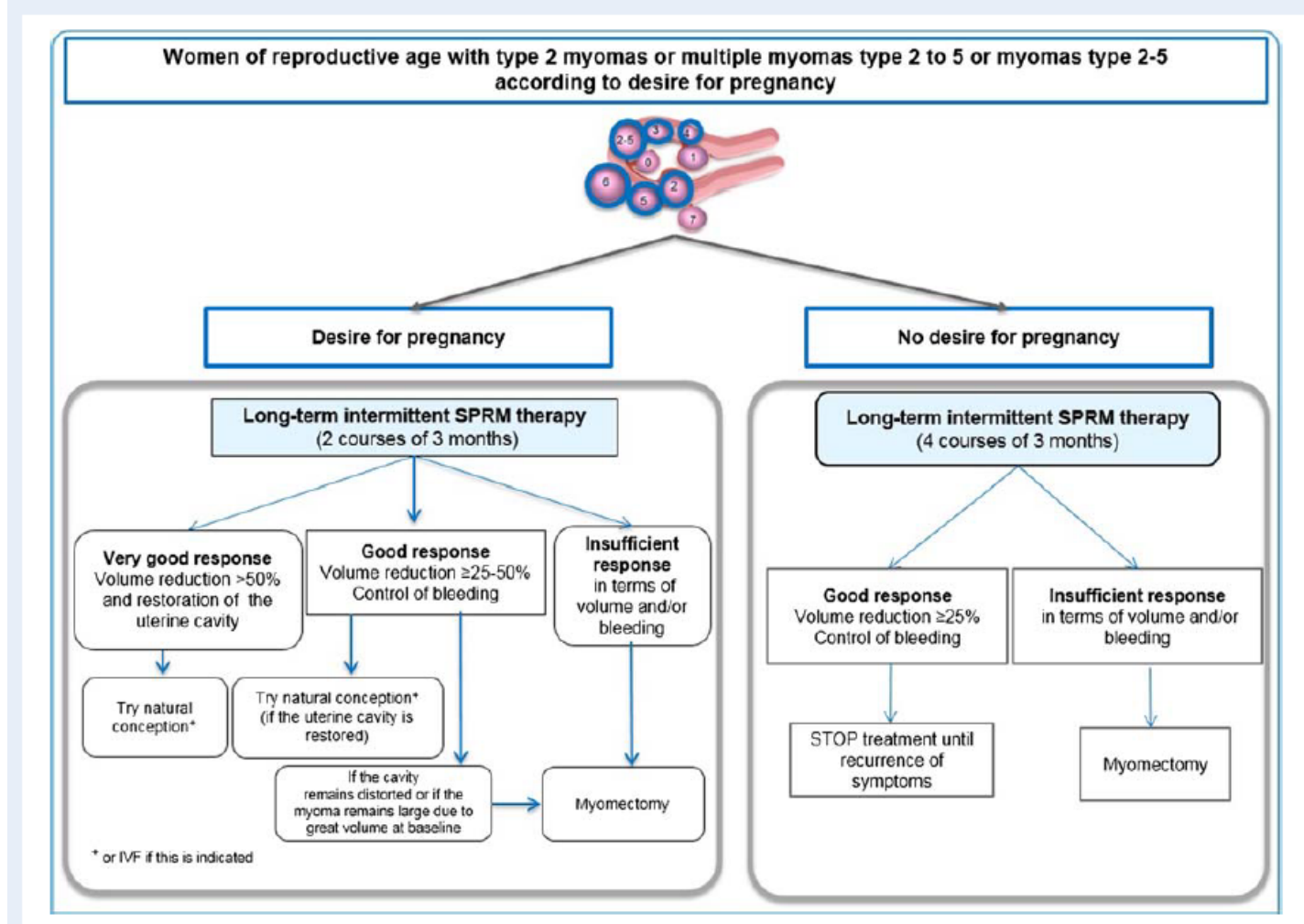
2012



### Quale tecnica chirurgica per migliorare gli outcome riproduttivi?



Caesarean section rate non è influenzata dalla tecnica chirurgica



**Figure 9** Management in case of myomas or multiple myomas (type 2–5) in women of reproductive age, according to desire for pregnancy. In cases of infertility, two courses of three months are recommended (left panel). Subsequent therapy is determined depending on the response to treatment and restoration of the uterine cavity. If there is no desire to conceive (right panel), long-term (four courses) intermittent therapy may be proposed. In case of a good response in terms of fibroid volume reduction and bleeding, treatment is stopped and only restarted if symptoms recur. Fibroid classification cartoon republished with permission from [Munro et al. \(2011\)](#).

# Impact on fertility

TABLE 2				
Effect of fibroids on fertility: all locations.				
Outcome	Number of studies/substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	18	0.849	0.734–0.983	$P=.029$
Implantation rate	14	0.821	0.722–0.932	$P=.002$
Ongoing pregnancy/live birth rate	17	0.849	0.734–0.983	$P=.029$
Spontaneous abortion rate	18	1.000	0.734–1.366	Not significant
Preterm delivery rate	3	1.000	0.309–3.160	Not significant

*Pritts. Fibroids and infertility. Fertil Steril 2009.*

## Fibroids and infertility: an updated systematic review of the evidence

Elizabeth A. Pritts, M.D.,<sup>a</sup> William H. Parker, M.D.,<sup>b</sup> and David L. Olive, M.D.<sup>a</sup>

TABLE 5				
Effect of fibroids on fertility: intramural fibroids.				
Outcome	Number of studies/substudies	Relative risk	95% confidence interval	Significance
<b>A. All studies</b>				
Clinical pregnancy rate	12	0.810	0.696–0.941	$P=.006$
Implantation rate	7	0.684	0.587–0.796	$P<.001$
Ongoing pregnancy/live birth rate	8	0.703	0.583–0.848	$P<.001$
Spontaneous abortion rate	8	1.747	1.226–2.489	$P=.002$
Preterm delivery rate	1	6.000	0.309–116.606	Not significant
<b>B. Prospective studies</b>				
Clinical pregnancy rate	3	0.708	0.437–1.146	Not significant
Implantation rate	2	0.552	0.391–0.781	$P=.001$
Ongoing pregnancy/live birth rate	2	0.465	0.291–0.744	$P=.019$
Spontaneous abortion rate	2	2.384	1.110–5.122	$P=.002$
Preterm delivery rate	0	—	—	—
<b>C. Studies using hysteroscopy in all subjects</b>				
Clinical pregnancy rate	2	0.845	0.666–1.071	Not significant
Implantation rate	1	0.714	0.547–0.931	$P=0.013$
Ongoing pregnancy/live birth rate	2	0.733	0.383–1.405	Not significant
Spontaneous abortion rate	2	1.215	0.391–3.774	Not significant
Preterm delivery rate	1	6.000	0.309–116.606	Not significant

*Pritts. Fibroids and infertility. Fertil Steril 2009.*

Relative risk	95% confidence interval	Significance
0.737	0.649–0.850	$P=.005$
0.649	0.580–0.722	$P=.003$
0.850	0.722–1.000	$P=.001$
2.051	1.226–3.428	$P=.002$
—	—	—

Outcome	Number of studies/substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	14	0.897	0.800–1.004	Not significant
Implantation rate	14	0.792	0.696–0.901	$P<.001$
Ongoing pregnancy/live birth rate	16	0.780	0.690–0.883	$P<.001$
Spontaneous abortion rate	16	1.891	1.473–2.428	$P<.001$
Preterm delivery rate	2	2.767	0.797–9.608	Not significant

*Pritts. Fibroids and infertility. Fertil Steril 2009.*



# Removal of myomas in asymptomatic patients to improve fertility and/or reduce miscarriage rate: a guideline

Practice Committee of the American Society for Reproductive Medicine

The American Society for Reproductive Medicine, Birmingham, Alabama

- Non ci sono evidenze sufficienti per concludere che la presenza di miomi riduca la probabilità di gravidanza con o senza trattamenti per la fertilità (grado C)
- Non ci sono evidenze sufficienti per determinare chiaramente quali tipi di mioma abbiano maggiore impatto sulla fertilità e sul rischio di aborto spontaneo
- Non ci sono evidenze sufficienti che la rimozione dei miomi sottosierosi migliori la fertilità (grado C)
- Ci sono evidenze che la miomectomia non migliori in maniera statisticamente significativa il tasso di successo di ART. (grado B)
- Non ci sono evidenze sufficienti che la miomectomia laparoscopica o laporotomica riduca il tasso di aborto spontaneo.
- Ci sono evidenze sufficienti per affermare che la miomectomia isteroscopica migliori il *clinical pregnancy rates* (grado B)
- Viceversa, non ci sono evidenze per affermare che tale procedura riduca il rischio di aborto spontaneo. (grado C)

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Medicine  
<http://dx.doi.org/10.1016/j.fertnstert.2017.06.034>



# Removal of myomas in asymptomatic patients to improve fertility and/or reduce miscarriage rate: a guideline

Practice Committee of the American Society for Reproductive Medicine

The American Society for Reproductive Medicine, Birmingham, Alabama

## RACCOMANDAZIONI:

- In donne asintomatiche con miomi CHE ALTERANO LA CONFORMAZIONE DELLA CAVITÀ UTERINA la miomectomia (laparoscopica, laparotomica o isteroscopica) può essere presa in considerazione per migliorare il tasso di successo riproduttivo.
- La miomectomia solitamente non è consigliata per aumentare il tasso di successo riproduttivo in donne infertili asintomatiche con miomi che non distorcono la cavità uterina.





# Reintervention risk and quality of life outcomes after uterine-sparing interventions for fibroids: a systematic review and meta-analysis

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**Objectives:** To compare uterine-sparing treatment options for fibroids in terms of reintervention risk and quality of life.

**Design:** Systematic review and meta-analysis according to PRISMA guidelines.

**Setting:** Not applicable.

**Patient(s):** Women with uterine fibroids undergoing a uterine-sparing intervention.

**Interventions(s):** Not applicable.

**Main Outcome Measure(s):** 1) Reintervention risk after uterine-sparing treatment for fibroids after 12, 36, and 60 months; and 2) quality of life outcomes, based on validated questionnaires. Two separate analyses were performed for the procedures that used an abdominal approach (myomectomy, uterine artery embolization [UAE], artery ligation, high-intensity focused ultrasound [HIFU], laparoscopic radiofrequency ablation [RFA]) and for the procedures managing intracavitary fibroids (hysteroscopic approach, including hysteroscopic myomectomy and hysteroscopic RFA).

**Result(s):** There were 85 articles included for analysis, representing 17,789 women. Stratified by treatment options, reintervention risk after 60 months was 12.2% (95% confidence interval [CI] 5.2%–21.2%) for myomectomy, 14.4% (95% CI 9.8%–19.6%) for UAE, 53.9% (95% CI 47.2%–60.4%) for HIFU, and 7% (95% CI 4.8%–9.5%) for hysteroscopy. For the other treatment options, no studies were available at 60 months. For quality of life outcomes, symptoms improved after treatment for all options. The HIFU procedure had the least favorable outcomes.

**Conclusion(s):** Despite the substantial heterogeneity of the study population, this meta-analysis provides valuable information on relative treatment efficacy of various uterine-sparing interventions for fibroids, which is relevant when counseling patients in daily practice. Furthermore, this study demonstrates that long-term data, particularly for the newest uterine-sparing interventions, are urgently needed. (Fertil Steril® 2018;109:698–707. ©2017 by American Society for Reproductive Medicine.)

**Key Words:** Reintervention risk, quality of life, uterine-sparing treatment option

**Discuss:** You can discuss this article with its authors and other readers at <https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/23404-24254>.



# Perspectives of Obstetricians on Labour and Delivery After Abdominal or Laparoscopic Myomectomy

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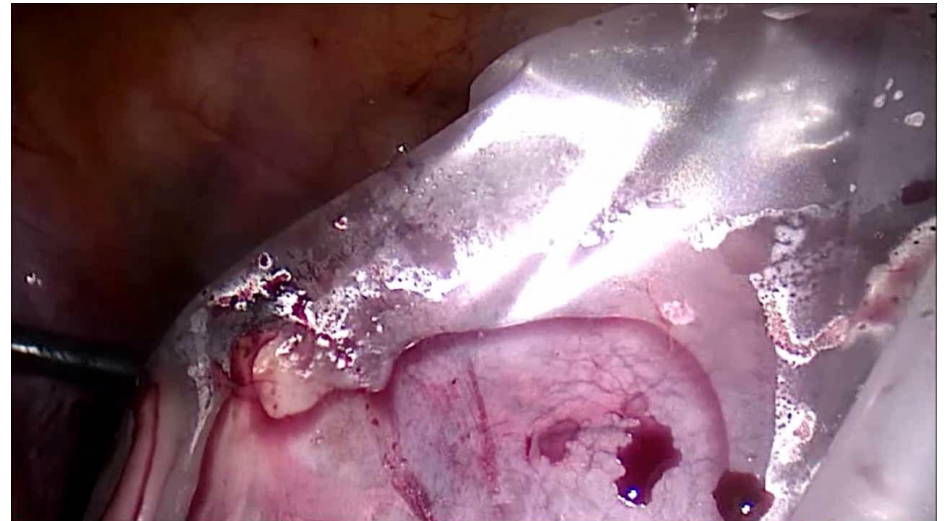
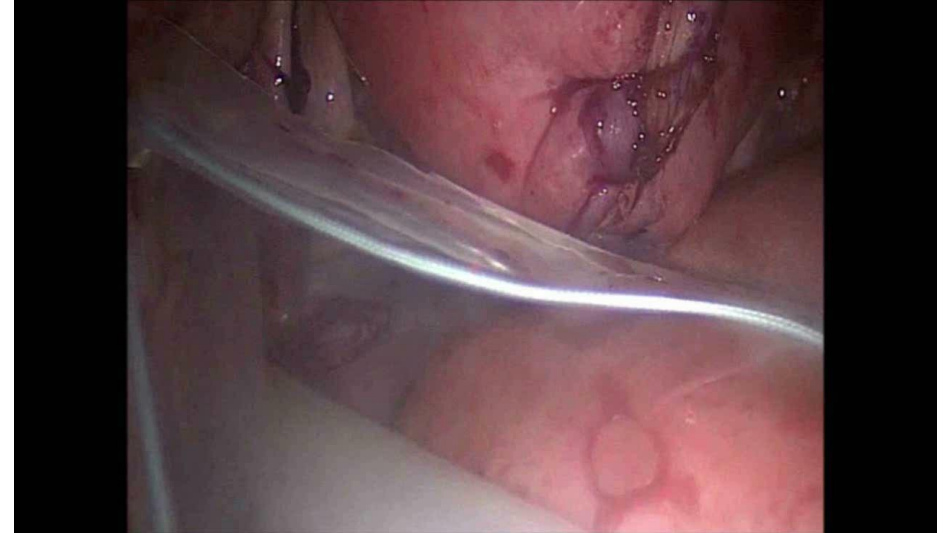
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Survey a medici che si occupano soprattutto di Ostetricia,  
2014



# Alternatives and Other Approaches to Morcellation

- For women undergoing hysterectomy for benign disease, the American College of Obstetricians and Gynecologists recommends a minimally invasive approach whenever feasible.
- **Alternative to power morcellation**
- morcellation through suprapubic or umbilical incisions with containment bags
- hand-assisted morcellation through a mini-laparotomy
- vaginal morcellation



# Before Surgery

## MEDICAL THERAPY

- Purpose >
  - stop bleeding
  - correct anemia
  - improve the quality of life
  - decrease the volume of the leiomyomas.
- The surgical approach can be changed if the uterine volume decreases significantly, making a laparoscopy route possible when a laparotomy was scheduled initially.
- Two medical therapies have proven to be effective in this indication:
- GnRHa and SPRM (ulipristal acetate).
- Valaprisan, a novel promising powerful SPRM, is currently under investigation in phase III studies.

